

## **Remarks**

Claims 53-74 are pending in the application and stand rejected. Claims 53, 54, 55, 57-61, 63, 64, and 67-74 are amended, and claims 1-52, 56, 62, 65, and 66 have been cancelled. New claims 75-82 have been added. Support for new claim 75 can be found in the Specification at page 12, lines 26-28; at page 4, line 4-10; page 13, lines 6-10; page 13, line 22-page 14, line 8; and Figures 6 and 9. Support for new claims 76 and 79 can be found in the Specification at page 13, line 23, through page 14, line 8 and in the parent application U.S.S.N. 09/253,153 (as published as US 2002/006604), which has been incorporated by reference into the present application, in Figure 1 and 2 and paragraphs [0091]-[0092]. Support for new claim 77 can be found at page 4, line 4-10; page 13, lines 6-10; page 13, line 22-page 14, line 8; and Figures 6 and 9 of the Specification. Support for claim 78 can be found on page 13, line 22, through page 14, line 8 of the Specification of the present application. Support for claim 80 can be found on page 11, lines 13-17 of the Specification. Support for claim 81 can be found on page 11, lines 3, and 19-25 and in Figure 3. Support for new claim 82 can be found on page 11, lines 27-29. Applicant submits that no new matter has been added by these amendments. Applicant respectfully requests reexamination and reconsideration of the case, as amended. Each of the rejections levied in the Office Action is addressed individually below.

### **I. Election/Restriction**

The Examiner has withdrawn claims 53-64 and 67-74 as being directed to a non-elected invention. Applicant has amended the pending claims to recite “proteins and peptides” rather than “chemical compounds.” This amendment places all pending claims within the elected invention.

### **II. Information Disclosure Statement**

Examiner has requested a copy of the publication entitled “All-in-One Synthesis and Evaluation” *Analytical Chemistry*, p. 789A, December 1, 1999, which was cited in the IDS filed February 19, 2004. Applicant includes herewith a copy of the requested publication as well as a PTO Form 1449 listing the reference. Applicant requests that the Examiner consider the

publication and initial the enclosed Form as evidence that the publication has been fully considered by the Examiner. Applicant apologizes for mistakenly not including a copy of this reference with the last submission.

### **III. Claim Objections**

Applicant has renumbered the claims as requested by the Examiner.

Claims 65 and 66 were objected to by the Examiner for depending from withdrawn claims. Applicant has amended all claims so that they fall within the elected invention. Applicant submits that the present amendment renders the objection to claims 65 and 66 moot.

### **IV. Rejections under 35 U.S.C. § 112, first paragraph**

The Examiner rejected claims 65 and 66, insofar as claims 65 and 66 depend from claims 53 and 57, under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. The Examiner states that the claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

With respect to claims 65 and 66, as they depend from claim 53, the Examiner maintains that there is not support for the language that the members of a library are synthesized “so that a larger number of products is produced than different chemical reactions are performed.” This language is supported by the discussion of combinatorial chemistry found in the specification. *See, e.g.*, page 2, lines 5-26. One of the advantages of combinatorial chemistry is the wide range of chemical compounds one is able to prepare as compared to the number of synthetic steps performed. In traditional synthetic organic chemistry, a starting material is taken through a series of reaction steps to accomplish the synthesis of one desired product. In certain instances, the synthesis may require 5-20 steps to produce one compound. In combinatorial chemistry, *e.g.*, split-and-pool synthesis, a starting material is attached to solid supports, the solid supports are split into groups, each of which is subjected to different reaction conditions. The supports are then pooled and split up again yielding a second set of groups, each of which is subjected to

another set of reaction conditions. The solid supports are pooled and split up again. The resulting third set of groups is subjected to yet another set of reaction conditions. This splitting and pooling may be repeated numerous times to increase the diversity and complexity of the growing library of compounds. Using combinatorial chemistry hundreds to thousands of compounds can be prepared quickly without laboriously having to synthesize each compound one-by-one. The number of reactions needed to obtain the compounds in a combinatorial library using split-and-pool synthesis is much less than the number of reactions that would need to be performed if traditional synthetic methods were used to prepare each compound of the library. For example, a combinatorial library with 25 members can be prepared using just ten reactions—five reactions in each of two split-and-pool steps, whereas fifty reaction would be required to produce the 25 products using traditional one-by-one organic synthesis. This aspect of combinatorial chemistry is appreciated by those of skill in this art and would have been appreciated as applicable to the claimed invention in the present case. Furthermore, support for this language can be found in the parent application U.S.S.N. 09/253,153, which has been incorporated by reference into the CIP application, on page 1, lines 20-23 (see paragraph [0003] of the published application US 2002/0006604). Therefore, the language of claim 53 does not constitute new matter, and the Applicant requests that the rejection be removed.

With respect to claims 65 and 66, as they depend from claim 57, the Examiner states that support for the limitations that the members of a library are related to one another by “synthetic history” and wherein each member of a first subset is separated from each “next closest member by a first distance” does not appear in the specification as originally filed. In addition to the portion of the parent application USSN 09/253,153 referred to in the last Response, the Examiner is directed to Figures 1 and 2 of the parent application. Referring to Figure 1, the linear array shown in Figure 1D with ABCABCABCABC written above the fiber could represent an optical fiber in which A, B, and C each represent a particular amino acid residue. For example, region A may represent peptides with a tyrosine residue at position 1 of the peptide’s primary sequence, region B may represent peptides with a proline residue at position 1 of the peptide’s primary sequence, and region C may represent peptides with a serine residue at position 1 of the peptide’s

primary sequence. Therefore, the regions of the fiber with peptides containing tyrosine at position 1 are separated by a fixed distance.

Continuing, if one refers to Figure 2C, the D, E, and F represent amino acids found at position two of a peptide's primary sequence. For example, D may represent phenylalanine, E may represent alanine, and F may represent lysine. Therefore, a peptide falling within the AD region of the fiber would have a tyrosine at position 1 and a phenylalanine at position 2. Again, as shown in the Figure 2, regions with phenylalanine at position 2 are separated by a constant distance.

One of ordinary skill in this art reviewing specification of the parent application, particularly, page 4, lines 14-18; page 7, line 26-page 8, line 7; page 9 line 25-page 11, line 3; page 18, line 1-page 26, line 6, and Figure 1 and 2 would understand that the inventors had possession of claimed invention in claim 57 at the time of filing. Applicant, therefore, requests that the rejection be withdrawn.

#### **V. Rejections under 35 U.S.C. § 112, second paragraph**

The Examiner has rejected claims 65 and 66, insofar as claims 65 and 66 depend from claims 53 and 57, under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 65 and 66, insofar as they depend from claim 53, are rejected for the language "can be generated" which the Examiner maintains renders the claims vague and indefinite. Claim 53 has been amended to recite "are generated" rather than "can be generated" so that it is clear that members of the combinatorial library are generated via the chemical reaction recited in the claims. Applicant submits that amended claim 53 is definite and clear and requests that the rejection be withdrawn.

Claims 66 and 67, insofar as they depend from claim 57, are rejected for the language "synthetic history" which the Examiner maintains renders the claims vague and indefinite. As explained in more detail above in the section entitled "Rejection under 35 U.S.C. § 112, first paragraph," the synthetic history of a peptide or protein refers to the incorporation of amino acids

into the primary sequence of the peptide or protein. All members of a given subset of peptides or proteins will have the same amino acid residue at a particular position of the primary sequence. One of skill in the art would understand this term in light of the Example in the parent application. Therefore, Applicant respectfully submits that claim 57 and its dependencies are definite as written and requests that the rejection be removed.

#### **VI. Rejections under 35 U.S.C. § 102**

Claims 65 and 66, insofar as they depend from claims 53 and 57, stand rejected by the Examiner under 35 U.S.C. § 102(e) as being anticipated by Stimpson, U.S. Patent 6,037,186. Examiner states that Stimpson discloses combinatorial peptide compounds and combinatorial libraries, which form array of protein compounds linearly arranged in two dimensional arrays on microporous materials that are glass or other materials. These materials are rolled into rods or bundles that encompass optical fibers because they are capable of transmitting or guiding light. Even if Stimpson teaches what the Examiner has described, Stimpson does not anticipate the claimed invention because of Stimpson does not teach linear arrays of peptides or proteins on an optical fiber.

The claimed invention is a linear (one dimensional) array of peptides or proteins along an optical fiber. In order for Stimpson to anticipate the claimed invention, Stimpson must teach all elements of the claimed invention. Stimpson fails to teach or disclose several aspects of the claimed invention. Stimpson describes two-dimensional arrays (col. 3, line 36-37), not one-dimensional arrays. In column 4, lines 5-7, Stimpson clearly indicates that the rod is exposed to the compound “to allow uniform attachment throughout its length (Z axis).” Each rod has bound to it one binding agent, not an array of agents, as claimed in the present application. Stimpson’s invention allows for the production of multiple copies of a two-dimensional array by cutting slices of a bundle of rods perpendicular to the Z-axis of the bundle (col. 4, lines 30-31). Stimpson does not teach the arraying of a library of peptides or proteins along a single linear optical fiber; therefore, Stimpson does not anticipate the claimed invention. Applicant requests that the rejection be removed given the substantial differences between the claimed invention and the disclosure of Stimpson.

**V. Rejections under 35 U.S.C. § 103**

Claims 65 and 66, insofar as they depend from claim 53, are rejected under 35 U.S.C. § 103(a) as being unpatentable over being unpatentable over Browne *et al.* (*Anal. Chem.* 1996) and Pirrung *et al.* (U.S. Patent 5,143,854). Claim 53 has been amended to include a geometrical substrate about which the optical fiber is wrapped in a spiral and in a single layer of fiber about the substrate so that the fiber can be exposed to chemical reagents used in preparing the library members. As the Examiner says in the latest Office Action, neither Browne *et al.* nor Pirrung *et al.* teach the wrapping of the fiber about a geometric substrate. Therefore, the amended claim 53 is not rendered obvious by the combination of Browne *et al.* and Pirrung *et al.*

The Examiner later cited Myers *et al.*, U.S. Patent 4,848,687, in the rejection of claim 54 for the teaching of winding the optical fiber on a spool for storage. However, even Myers *et al.* in combination with Browne *et al.* and Pirrung *et al.* cannot render obvious the claimed invention because anyone storing a fiber on a spool would necessarily wrap the fiber around the spool in multiple layers to conserve storage space. In the amended claim, the fiber is wrapped in a single layer in order to have the fiber largely exposed to the reaction conditions for preparing the array. Therefore, the combination of Browne *et al.*, Pirrung *et al.*, and Myers *et al.* do not render the claimed invention obvious.

Claims 65 and 66, insofar as they depend from claim 57, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Browne *et al.*, Pirrung *et al.*, and Pilevar *et al.* (*Anal. Chem.* 1998). Claims 57 has also been amended line claim 53 to recite “the optical fiber is wrapped in a spiral and in a single layer of fiber about the substrate.” Therefore, the amended claim 57 is not rendered obvious by the combination of Browne *et al.*, Pirrung *et al.*, and Pilevar *et al.* In addition, as discussed above, even if Myers *et al.* is added to the combination, it will not render claim 57 as amended obvious.

Claims 65 and 66, insofar as they depend from claim 54, are rejected under 35 U.S.C. § 103(a) as being unpatentable over Browne *et al.* and Pirrung *et al.* and further in view of Myers *et al.*, U.S. Patent 4,848,687. The Examiner states that Myers *et al.* teaches the winding of an optical fiber on a spool for storage. In the present invention, the optical fiber is wrapped about a

geometric substrate in order to facilitate the preparation of the peptides/proteins on the array. The fiber is not wrapped around the substrate for storage purposes. Therefore, there would have been no motivation to combine Myers *et al.* with Browne *et al.* and Pirrung *et al.* Without a teaching or suggestion to combine the cited references, the Examiner has not established a *prima facie* case of obviousness, and Applicant requests that the rejection be removed.


However, solely to further prosecution, the Applicant has amended claim 54 to recite “the optical fiber is wrapped in a spiral and in a single layer of fiber about the substrate.” Support for this amendment can be found in the originally filed Specification at page 4, line 4-10; page 13, lines 6-10; page 13, line 22-page 14, line 8; and Figures 6 and 9. The amendment further distinguishes the claimed invention from the combination of the three references. Clearly, one wishing to store a fiber on a spool would not wrap the fiber about the substrate in a single layer but instead would wrap the fiber about the substrate in multiple layers thereby conserving space. Storage of anything necessarily implies a maximum amount of material in a minimum amount of space. However, in the instant invention, the surface of the fiber must be accessible to the reagents/solvent needed in preparing the proteins/peptides on the fiber. Therefore, only a single layer about the substrate would work in the claimed invention. Applicant submits that the claimed invention as amended is not rendered obvious by the combination of Browne *et al.*, Pirrung *et al.*, and Myers *et al.* Applicant requests that the rejection be removed.

Furthermore, Applicant respectfully points out that the scientific community has embraced the inventive arrays as truly novel and distinct. The Examiner has agreed that the commentaries provided with the last Response support the Applicant’s position but continues that Czarnik’s and Terrett’s commentaries are not conclusive because the relationship of the chemistry procedures or techniques commented upon and the claimed invention is not clear. The Examiner specifically mentions that Czarnik and Terrett do not discuss arrays on optical fibers. Although they do not discuss arrays on optical fibers specifically, what these commentator do recognize is the value of arraying and analyzing chemical libraries such as peptides or proteins in one dimension. The importance and advantages of this system stand whether the arrays are on optical fibers or strings; therefore, the submitted commentaries are directly applicable to the claimed invention.

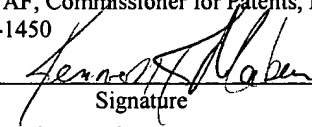
In view of the forgoing arguments, Applicant respectfully submits that the present case is now in condition for allowance. A Notice to that effect is requested.

Please charge any fees that may be required for the processing of this Response, or credit any overpayments, to our Deposit Account No. 03-1721.

Respectfully submitted,

  
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